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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,323	08/01/2005	Christopher Robin Lowe	GJE-7169	5107

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SALIWANCHIK LLOYD & SALIWANCHIK
A PROFESSIONAL ASSOCIATION
PO BOX 142950
GAINESVILLE, FL 32614-2950

EXAMINER	
SCHUBERG, LAURA J	

ART UNIT	PAPER NUMBER
1657	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,323	LOWE ET AL.	
	Examiner	Art Unit	
	LAURA SCHUBERG	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *23-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I (claims 1-22) in the reply filed on 11/05/2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-35 are pending.

Claims 23-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/05/2007.

Claims 1, 3, and 19 have been amended.

Claims 1-22 have been examined on the merits.

Previous Rejections

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Response to Amendment

The affidavit filed on 08/26/2008 under 37 CFR 1.131 has been considered but is ineffective to overcome the Jensen et al reference.

The evidence submitted is insufficient to establish diligence from a date prior to the date of reduction to practice of the Jensen et al reference to either a constructive reduction to practice or an actual reduction to practice. While Applicant has provided some evidence (exhibit A) which may demonstrate conception and with the filing of the foreign application-constructive reduction to practice, evidence of diligence has not been provided.

An applicant must account for the entire period during which diligence is required. Gould v. Schawlow, 363 F.2d 908, 919, 150 USPQ 634, 643 (CCPA 1966) (Merely stating that there were no weeks or months that the invention was not worked on is not enough.); In re Harry, 333 F.2d 920, 923, 142 USPQ 164, 166 (CCPA 1964) (**statement that the subject matter "was diligently reduced to practice" is not a showing but a mere pleading**). A 2-day period lacking activity has been held to be fatal. In re Mulder, 716 F.2d 1542, 1545, 219 USPQ 189, 193 (Fed. Cir. 1983) (37 CFR 1.131 issue); Fitzgerald v. Arbib, 268 F.2d 763, 766, 122 USPQ 530, 532 (CCPA 1959) (Less than 1 month of inactivity during critical period. Efforts to exploit an invention commercially do not constitute diligence in reducing it to practice. An actual reduction to practice in the case of a design for a three-dimensional article requires that it should be embodied in some structure other than a mere drawing.); Kendall v. Searles, 173 F.2d 986, 993, 81 USPQ 363, 369 (CCPA 1949) (Diligence requires that applicants must be specific as to dates and facts.)- MPEP 2138.06.

In addition, the missing signature of one of the inventors has not been properly addressed. According to MPEP 715.04, where one or more of the named inventors of

the subject matter of the rejected claim(s) (who had originally signed the oath or declaration for patent application under 37 CFR 1.63) is now unavailable to sign an affidavit or declaration under 37 CFR 1.131, the affidavit or declaration under 37 CFR 1.131 may be signed by the remaining joint inventors provided a petition under 37 CFR 1.183 requesting waiver of the signature of the unavailable inventor be submitted with the affidavit or declaration under 37 CFR 1.131. Proof that the non-signing inventor is unavailable or cannot be found similar to the proof required for a petition under 37 CFR 1.47 must be submitted with the petition under 37 CFR 1.183 (see MPEP § 409.03(d)). Petitions under 37 CFR 1.183 are decided by the Office of Petitions (see MPEP § 1002.02(b)).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-5, 7-11, 13-16, 19-22 remain rejected under 35 U.S.C. 102(e) as being anticipated by Jensen et al (US 2004/0077075).

Claim 1 is drawn to a method for monitoring cells in a microfluidic device comprising: feeding the cells into the microfluidic device through one or more microfluidic channels, wherein the device includes a chamber comprising a sensor; and monitoring the cells under conditions such that attachment of the cells to the surface of the chamber is inhibited.

Dependent claims include wherein the chamber surface comprises a gas-permeable material (claim 2); wherein the gas is selected from a group (claim 3); wherein the material is a fluoropolymers (claim 4); wherein the chamber surface comprises a hydrophilic material (claim 5); wherein the chamber is formed in epoxy resin coated on a plastics substrate (claim 7); wherein the plastics substrate is polycarbonate (claim 8); wherein the chamber comprises a plurality of sensors (claim 9); wherein the sensor is sensitive to oxygen, carbon dioxide, ammonium or pH (claim 10); wherein the sensor is optical or electrochemical or acoustic (claims 11 and 13); wherein the sensor is sensitive to a reactant or product of fermentation (claim 14); wherein the volume of the chamber is from 50 nL to 10 μL (claim 15); further comprising introducing growth medium into the chamber, wherein the sensor is sensitive to a reactant or product of cell growth (claim 16); further comprising introducing a component derived from the cells into a second microfluidic chamber comprising a sensor and in connection with the first chamber detecting the component (claim 19); wherein the component is a product of cell growth (claim 20); wherein the component is an expressed protein or enzyme (claim 21) and wherein the sensor of the second chamber is as defined in any of claims 10-15 (claim 22).

Jensen et al teach a microfluidic device for use in monitoring and culturing cells. The microfluidic device is a vessel having an interior volume of less than 200 ml and in particular 5 ml (page 3 para50) and which has an aeration membrane made of a fluoropolymer or silicone that allows oxygen diffusion to the growing cells (page 8 para 94). The surface of the chamber is modified to inhibit attachment of cells (page 8 para 97-99) and at least one analytical sensor is integrated into the device (page 10 para 112). Wherein the chamber surface comprises a hydrophilic material is taught (page 8 para 98-99) as well as wherein the chamber comprises a plurality of sensors, including optical and electrochemical (page 11 para 116) that are sensitive to oxygen, carbon dioxide or pH (page 11 para 117-127). The chamber is formed in an epoxy resin coated on a plastics substrate (page 18 para 206) and the substrate material includes polycarbonate (page 4 para 62). The analytical sensor detects or measures (is sensitive to) any cell metabolite or cell product such as a protein or enzyme (page 10 para 112). Introducing growth medium into the chamber, wherein the sensor is sensitive to a product of cell growth, is taught (page 1 para 7) as well as introducing a component derived from the cells into a second microfluidic chamber comprising a sensor and connected by a membrane with the first chamber detecting the component (page 1 para 10).

Therefore, the teaching of Jensen et al anticipates Applicant's invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 6 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Jensen et al (US 2004/0077075) as applied to claims 1-5, 7-11, 13-16, 19-22 above, and further in view of Wada et al (WO 99/67639-from IDS).

Claim 6 is drawn to the method of claim 5 and includes wherein the hydrophilic material is polyvinyl alcohol.

Jensen et al teach the method of using the microfluidic device as described above and indicate that a number of different approaches may be employed to alter the adsorptive properties of the contacting surfaces of the device and provide a hydrophilic surface (page 8 para 98-99).

Jensen et al do not specifically teach the use of polyvinyl alcohol as a hydrophilic material.

Wada et al teach a method for monitoring cells with a microfluidic device. The prevention of attachment of the cells to the interior surface of the device is taught as desirable and accomplished in a variety of ways such as using PVA (polyvinylalcohol) coatings (page 25 line 31-page 26 line 7).

Therefore, one of ordinary skill in the art would have been motivated to use PVA as a coating on the surface of the microfluidic device of Jensen et al because Wada et al teach that a PVA coating is a suitable treatment to prevent cell attachment in a microfluidic device and Jensen et al teach the desire to prevent cell attachment as well. One of ordinary skill in the art would have had a reasonable expectation of success because both Jensen et al (page 8 para 95) and Wada et al (page 24 line 18) are using microfluidic devices of the same material (PDMS).

Therefore, the combined teachings of Jensen et al and Wada et al render obvious Applicant's invention as claimed.

Claim 12 and 22 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Jensen et al (US 2004/0077075) as applied to claims 1-5, 7-11, 13-16, 19-22 above, and further in view of Lowe et al (US 5,989,923).

Claim 12 is drawn to the method of claim 11, wherein the sensor is a holographic sensor.

Jensen et al teach the method of using the microfluidic device as described above and indicate that there is a need to integrate available sensor technology (page 3 para 49).

Jensen et al do not specifically teach the use of holographic sensors with the microfluidic device.

Lowe et al teach a holographic sensor for measuring analytes (column 11 lines 18-46). In particular the sensor has applications in detecting biologically secreted proteins or proteases and is capable of detecting bacteria.

Therefore, one of ordinary skill in the art would have been motivated to apply the holographic sensors of Lowe et al to the microfluidic device of Jensen et al because Jensen et al indicate that more than one type of optical sensor may be used in the device to monitor cells (such as bacteria) and because Lowe et al teach that holographic sensors are suitable for optically interrogating bacteria. One of ordinary skill in the art would have had a reasonable expectation of success because Lowe et al teach that it is readily apparent that a holographic sensor may be fabricated whose characteristics are predictable (column 11 lines 22-25).

Therefore, the combined teachings of Jensen et al and Lowe et al render obvious Applicant's invention as claimed.

Claims 17 and 18 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Jensen et al (US 2004/0077075) as applied to claims 1-5, 7-11, 13-16, 19-22

above, and further in view of Walker et al (US 5,474,774) and Qian et al (Analytical Chemistry 2002).

Claim 17 includes wherein the growth medium comprises a non-metabolisable mannose analogue.

Claim 18 includes wherein the analogue is methyl α-D-mannopyranoside.

Jensen et al teach the method of using the microfluidic device as described above and indicate that different approaches may be employed in inhibiting the attachment of the cells (pages 9-10, para 107).

Jensen et al do not specifically teach the addition of a non-metabolisable analogue of mannose, such as methyl α-D-mannopyranoside.

Walker et al teach a method of inhibiting the adhesion of bacteria to devices, such as fermentation equipment, by applying an extract to a suitable medium to a surface having bacteria to disengage the bacteria from the surface (column 2 lines 32-49).

Qian et al teach that methyl α-D-mannopyranoside is a compound that inhibits the adhesion of bacteria to surfaces (page 1808, column 2).

Therefore, one of ordinary skill in the art would have been motivated to use the non-metabolisable analogue of methyl α-D-mannopyranoside as a compound to prevent bacterial adhesion in the device of Jensen et al because Walker et al teach that it is known in the art to add compounds that inhibit bacterial adhesion to a surface, such as a fermentation device, in a suitable medium and Qian et al teach that methyl α-D-mannopyranoside is capable of inhibiting bacterial adhesion. One of ordinary skill in the

art would have had a reasonable expectation of success because Jensen et al indicate that different approaches may be employed in inhibiting the attachment of the cells (pages 9-10, para 107).

Therefore, the combined teachings of Jensen et al., Walker et al and Qian et al render obvious Applicant's invention as claimed.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3, 9-12, 14, 16, 19, 20, remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 7, 8, and 14 of copending Application No. 10/520331. Although the conflicting claims are

not identical, they are not patentably distinct from each other because they disclose inventions with the same limitations. It is noted that instant claim 1 requires that the cell is inhibited from attachment to the surface of the chamber, whereas claim 1 of copending 10/520221 requires that the cell be immobilized. However these limitations do not exclude wherein a cell is immobilized on a bead that is then inhibited from attachment to the surface of the chamber. Therefore the claims, as recited, are overlapping.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAURA SCHUBERG whose telephone number is (571)272-3347. The examiner can normally be reached on Mon-Fri 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon B Lankford/
Primary Examiner, Art Unit 1651

Laura Schuberg